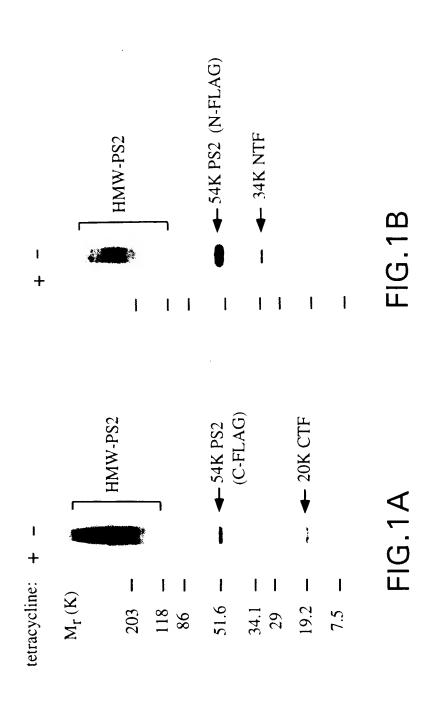
Appl. No. 09/065,902.; Group Art Unit. 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC.;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



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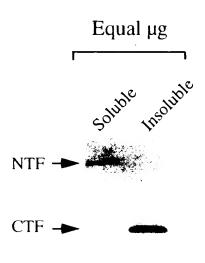
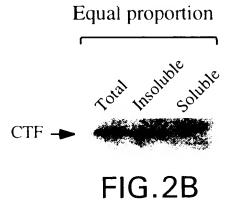


FIG.2A



Appl. No. 09/065,902;; Group Art Unit. 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

hrs 0 6 12 24 48 72

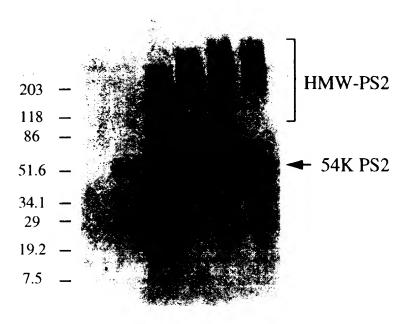


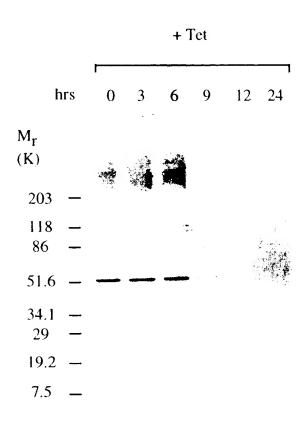
FIG.3A

hrs 0 6 12 24 48 72



FIG.3B

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title. Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



WT FIG.4A

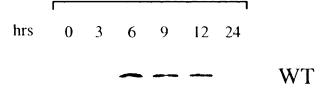


FIG.4B

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HI.K/PSC.;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

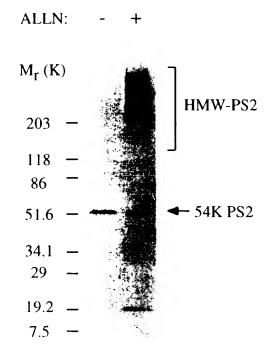


FIG.5A

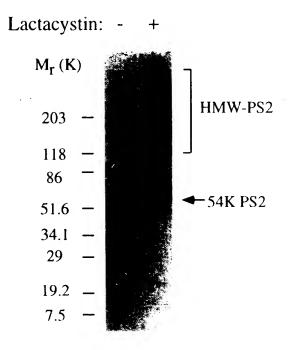


FIG.5A-1

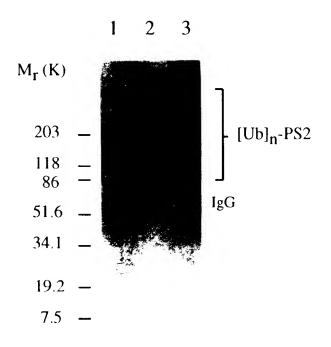
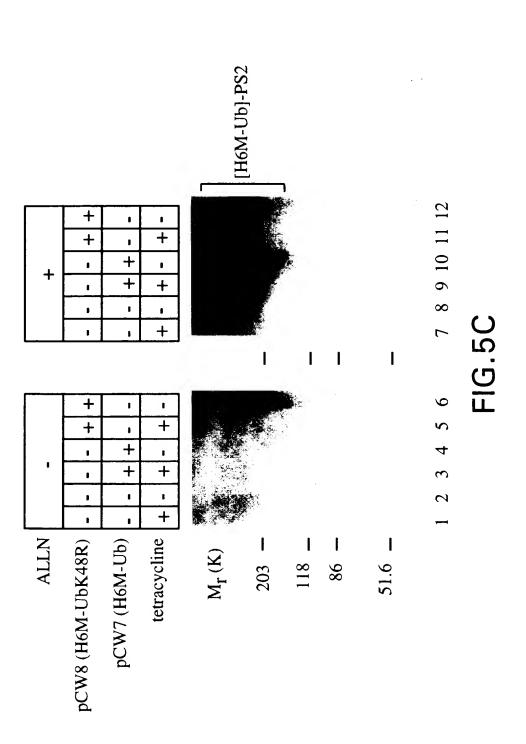


FIG.5B

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
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Inventors: TANZI and KIM; Tel: 202371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

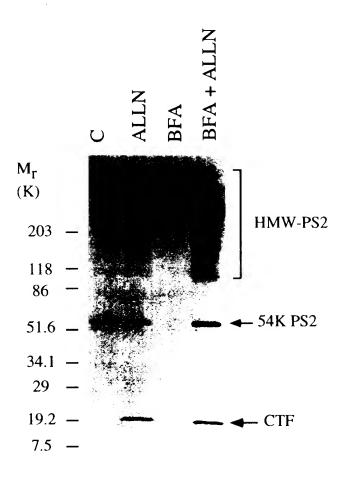
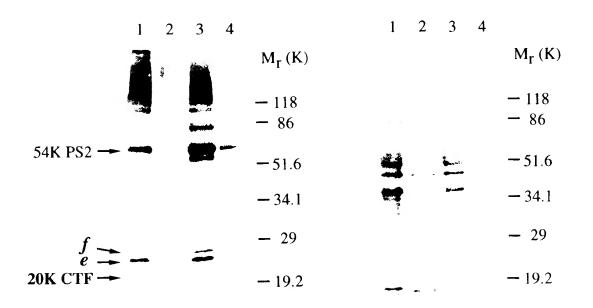


FIG.6

Appl. No. 09/065,902.; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title. Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

	1	2	tet:	+	_		
$M_{r}(K)$			$M_{r}(K)$				
118 – 86 –			203 —				
51.6 —			118 — 86 —				
34.1 – 29 –	*		51.6—			54K PS2	
19.2 —			34.1 —			f	
7.5 —			29 – 19.2 –		_ #	$\leq \frac{f}{e}$ 20K CTF	
αPS	2Loop	αPS2Loop	7.5 —				
		+ GST-HuPS2	F	FIG.7B			

FIG.7A



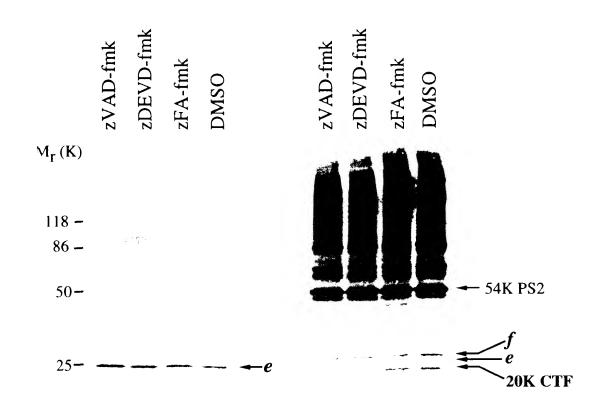
 $\alpha PS2Loop \\$

FIG.7C

Ponceau S

FIG.7C-1

Appl. No. 09/065,902;; Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



Uninduced

Induced

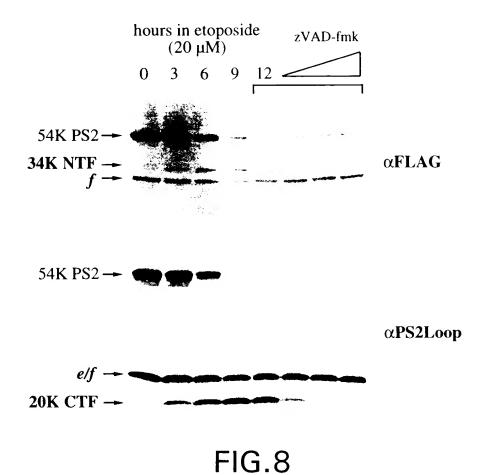
FIG.7D

FIG.7D-1

Appl. No. 09/065,902;; Group Art Unit: 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



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Inventors: TANZI and KIM; Tel. 2023/71-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

hours in STS (1 μ M) 0 3 6 9 12 24

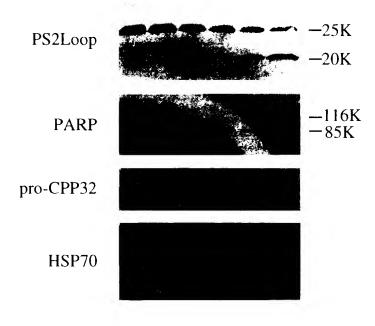
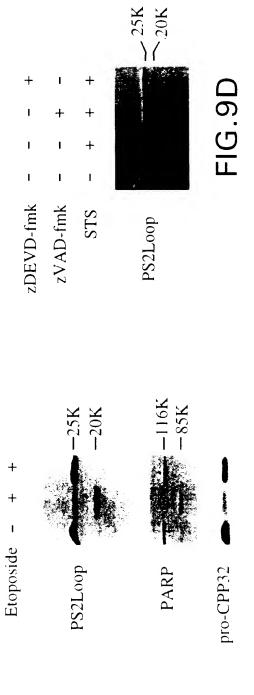


FIG.9A

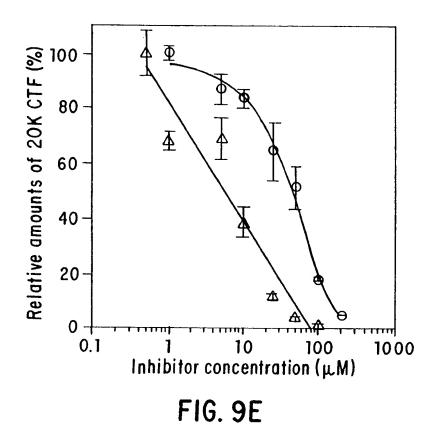
FIG.9B

Appl. No. 09/065,902;, Group Art Unit: 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC; ;
Inventors: TANZI and KIM; Tel. 202/371-2600
Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



zVAD-fmk -

Appl. No. 09/065,902,; Group Art Unit. 1644
Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel. 202/371-2600
Title: Purified 20 kDa Presenitin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenitin 2



Normal Cleavage Sites

296 Exon 10 323 A B Exon 11

//-PIFPALIYSSAMVWTVGMAKLDPSSQGALQLPYDPEMEEDSYDSFGEPSYPEVFE // PS2

D308A D326A D329A

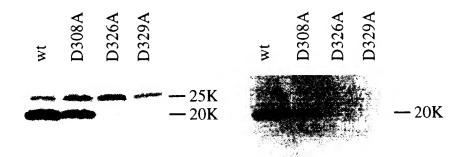
FIG. 10A

Appl. No. 09/065,902.; Group Art Unit: 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC,;

Inventors: TANZI and KIM; Tel: 202/371-2600

Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



αPS2Loop

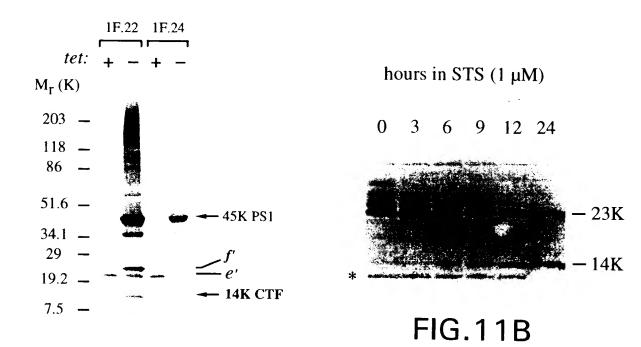
 $\alpha FLAG$

FIG.10B

Appl. No. 09/065,902;; Group Art Unit. 1644

Dkt. No. 0609/4270001/JAG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600

Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2



αPS1Loop

FIG.11A

FIG.11C

FIG.11D

Appl. No. 09/065,902;; Group Art Unit. 1644
Dkt. No. 0609/4270001/AG/HLK/PSC;;
Inventors: TANZI and KIM; Tel: 202/371-2600
Title Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

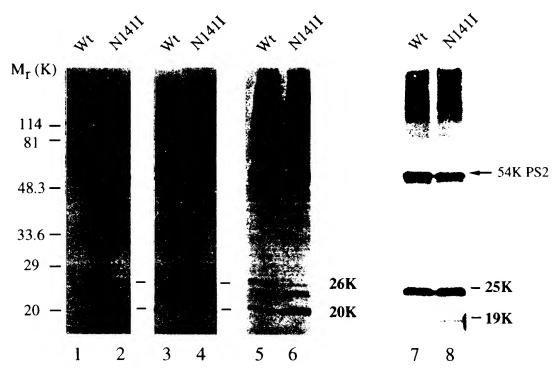


FIG.12A

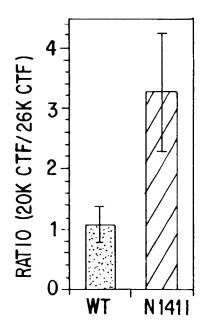


FIG.12B

Appl. No. 09/065,902;; Group Art Unit: 1644 Dkt. No. 0609/4270001/JAG/HI K/PSC; Inventors: TANZI and KIM; Tel: 202/371-2600 Title: Purified 20 kDa Presenilin 2 C-Terminal Fragment and Methods of Screening for Compounds That Inhibit Proteolysis of Presenilin 2

N1411 (Volga German) and D329A (Caspase Clip Site) N1411 (Volga German) and D329A (Caspase Clip Site) Establishment of Stable CHO Cell Lines Co-expressing APP and PS2 Containing Mutations

Establishment of Stable CHO Cell Lines Co-expressing APP and PS2 Containing

Mutations

N1411/D329A N1411

--Clone# 1 7

Normal CTI

FIG.13A Stable

IItIN N1411/D356

← Normal CTF ← Alt. CTF

Transient

FIG. 13B